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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/484,886	01/18/2000	Gale E. Smith	674506-2035.2	1236

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EXAMINER	
SRIVASTAVA, KAILASH C	
ART UNIT	**PAPER NUMBER**
1657	

MAIL DATE	DELIVERY MODE
05/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/484,886	SMITH ET AL.	
	Examiner	Art Unit	
	Dr. Kailash C. Srivastava	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *96-116 and 127-129* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *96-116 and 127-129* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Request for continued examination (i.e., RCE) under 37 CFR §1.114, including the fee set forth in 37 CFR §1.17(e), was filed in this application on 5 February 2007 after a Final action was mailed 30 December 2005. Since this application is eligible for continued examination under 37 CFR §1.114, and the fee set forth in 37 CFR §1.17(e) has been timely paid, the finality of the previous Office action mailed 22 February 2006 has been withdrawn pursuant to 37 CFR §1.114. Applicants' submission filed 05 February 2007 has been entered. Accordingly an RCE has been established and the action on RCE follows.

2. For the record, contrary to applicants' assertion at Page 5, Line 32 of the response accompanying aforementioned RCE filing, 5 January 2007 was a Friday, not a Monday. Furthermore, applicants' response was not filed on 5 January 2007, rather said response was filed on 05 February 2007.

3. Applicants' response and amendment filed 05 February 2007 to the Office Action mailed 30 December 2005 and to the Advisory Action mailed 25 July 2006 is acknowledged and entered.

4. The Art Unit Location for your application under prosecution at the United States Patent and Trademark Office (i.e., USPTO) has been changed to Art Unit 1657. To aid in correlating any papers for this application (i.e., 09/484,886), all further correspondence regarding this application should be directed to Examiner Kailash C. Srivastava in Art Unit 1657.

5. Please note that upon arrival at the USPTO, each response/filing is sorted according to claims, remarks, amendment, transmittal etc. for scanning coding and incorporation in to the Electronic File Wrapper (i.e., IFW). In order to ensure that all the papers pertaining to a particular application are properly coded in the same application electronic file wrapper, and to further facilitate the prosecution; especially during a telephonic conversation/interview with applicant/applicants' representative, it is suggested that the following information be recited in the header of each page for any filing/response/amendment filed in response to the instant Office Action:

a. U.S. Non-Provisional Application Serial Number (e.g. 00/000,000);
b. Filing date for said application (e.g., 17 November 2002);
c. First Applicant's name (e.g., Smith Jones et al.);
d. Attorney Docket Number;
e. Group Art Unit Number (e.g., 1657);

f. Examiner's name (e.g., Dr. Kailash C. Srivastava);

g. Date of Office Action being responded to (e.g., 27 August 2006); and

h. Date of amendment/response (e.g., 27 April 2007)

Papers/responses filed according to above-stated guidelines immensely ameliorate the chances of papers lost during transaction/transmission, coding, indexing and placing the papers in IFW.

CLAIMS STATUS

6. Claims 1-95 and 117-126 have been cancelled.

7. Claims 127-129 have been added.

8. Claims 96-116 and 127-129 are pending and are examined on merits.

Objection To Claims – Minor Informalities

9. Claims 96-116 and 127-129 are objected to because of the following informalities:

- Phrase, "relative homogeneity" at line three of claims 96 and 127-129 is objected because the comparative basis for "relative homogeneity" is unclear. Is the "relative homogeneity" of erythropoietin in comparison to another erythropoietin produced by another method or the non-recombinant erythropoietin, or the unpurified recombinant erythropoietin produced in the claimed product by process claims or what? Appropriate correction/clarification is required.

- Phrase, "has an *in vivo* activity and an activity of at least 200, 000 U/mg or of about 500,000 U/mg" at lines four to five of claim 96 is objected because said phrase renders those claims vague and incomprehensible. Is the activity *in vivo* and only *in vivo*, or said activity of 200,000 U/mg somewhere else? And which activity is it that is being claimed the 200,000 U/mg or 500,000 U/mg? Claim 96 as presented currently gives the connotation that the activity could be either 200,000 U/mg or 500,000 U/mg. Appropriate correction/clarification is required.

- Phrase, "has an *in vivo* activity and an activity of at least 200, 000 U/mg" at lines four to five of claim 96 and at Lines 2-3 of Claims 97-98 is objected to because said phrase

renders those claims vague and incomprehensible. Is the activity *in vivo* and only *in vivo*, or said activity of 200,000 U/mg somewhere else? Appropriate correction/clarification is required.

- Phrase 200,000 U/mg, or 500,000U/mg in Claims 96-98 and 127-129 are objected because it is not clear what the word "mg" refers to. The art- accepted activity definition in the context of the claimed invention is, " given amount (i.e., 200,000) U/mg protein. Appropriate correction is required.
- At Line 5 in Claim 103, the recitation, "desired" is objected to because it is not clear how one can determine with clarity and accuracy whose desire is to be practiced, when the "desire" is to be exercised and what are the metes and bounds of the word "desire"? Appropriate correction/clarification is required.
- Phrase "specific activity of "in Claims 127-129 is objected because the units of "specific activity" are improperly defined. The art- accepted specific activity definition in the context of the claimed invention is, " given amount (i.e., 200,000) U/mg protein. Appropriate correction is required.
- At line one of each of Claims 97-98 and 111-116, before the word "wherein" a --, -- should be inserted. Appropriate correction is required

All other claims depend directly from the objected claims (e.g., Claim 96) and are, therefore, also objected for the reasons set forth above.

Claim Rejections – 35 U.S.C. § 102

10. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> ***A person shall be entitled to a patent unless –***
>
> ***the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.***

11. Claims 96-97 and 99-116 and Newly presented Claims 127-129 are rejected under 35 U.S.C. §102(b) as anticipated by Quelle et al. (Blood. 1989. Volume 74, Pgs. 652-657) with evidence provided by Dorland's Illustrated Medical Dictionary (W.B. Saunders Co., Philadelphia, 1988, Page 581) for the reasons of record in the Office Action mailed 30 December 2005.

12. In response to art rejections under 35 U.S.C.§ 102(b) discussed supra, citing a number of case laws and applying said laws to the art rejection in the Office Action mailed 30 December 2005 and to the advisory mailed 25 July 2006, applicants argue "Quelle et al. fails to teach an erythropoietin purified to 95% or greater, having an *in vivo* activity." Applicants also argue that the "Examiner has misread Quelle et al. as to the *in vitro* activity shown by Quelle et al. such that Quelle et al. additionally fails to teach an erythropoietin purified to 95% or greater, having *in vitro* activity of at least 200, 000 U/mg or of about 500,000 U/mg (See applicants' remarks filed 5 February 2007, Page 6, Line 27 to Page 7, Line 3). Applicants further argue (See Applicants' Remarks filed 05 February 2007, Page 7, Lines 19-23) "The presently pending claims relate to a substantially pore, recombinant glycosylated erythropoietin, produced by a baculovirus expression system in cultured insect cells, wherein said erythropoietin has relative homogeneity or is purified to 95% or greater and said erythropoietin stimulates erythropoiesis and has an *in vivo* activity and an activity of at least 200, 000 U/mg or of about 500,000 U/mg."

Reiterating teachings from Quelle et al. reference cited in the Office Action mailed 30 December 2005 and the instantly claimed invention, the facts are as follows:

Claims in Instant Application Recite	**Quelle et al. (Blood, Volume 74, Pages 652-657, 1989), Especially Page 652, Column 1, Lines 6-25 and Column 2, Lines 6-13) Teach**
A recombinant, glycosylated ≥95 pure erythropoietin	A glycosylated, recombinant, ≥95 pure erythropoietin
Claimed erythropoietin is produced by a baculovirus expression system in cultured insect cells	Erythropoietin is obtained in cultured insect cells having a baculovirus expression system
Erythropoietin has an *in vivo* activity	Erythropoietin has some *in vivo* activity
Said erythropoietin stimulates erythropoiesis	Said erythropoietin stimulates erythropoiesis
The activity is at least 200,000 U/mg or of about 500,000 U/mg.	Erythropoietic activity is 200,000 U/mg

Additionally, giving the broadest interpretation of the claims as presented, the claimed erythropoietic activity is present *in vivo,* but the quantitative value claimed for the activity may or may not be *in vivo*. Furthermore, said quantitative activity is at least 200,000 U/mg or it may be 500, 000 U/mg. Therefore a reference teaching an activity of 200,000 U/mg still anticipates the claimed invention. Applicants, however, admit on record that Quelle et al's purified recombinant erythropoietin has "little activity in vivo" (See Applicants' response filed June 25, 2003). Applicants, without mentioning any

quantification of the claimed *in vivo* activity, or how said *in vivo* activity was quantified; further admit on record that the claimed "erythropoietin has an *in vivo* activity, however, the claimed activity of at least 200,000 U/mg or at least 500,000 U/mg was obtained during *in vitro* testing" (See Remarks, Page 7, Lines 17-24 in the Declaration from Mannon Cox Filed March 24, 2004). Therefore, the reference is deemed to anticipate the cited claims.

Applicants' arguments filed 05 February 2007 regarding the rejection to Claims 96-97 and 99-116 as anticipatory by Quelle et al. (Blood. 1989. Volume 74, Pgs. 652-657) with evidence provided by Dorland's Illustrated Medical Dictionary (W.B. Saunders Co., Philadelphia, 1988, Page 581)) in the Office Action mailed 30 December 2005 have been fully and carefully considered but are not persuasive for the reasons of record at pages 2-3, items 8-9 in the Office Action mailed 30 December 2005, additionally at item 11 in the Advisory Action mailed 25 July 2006, and those discussed *supra*.

Claim Rejections Under 35 U.S.C. § 103(a)

13. The following is a quotation of 35 U.S.C. §103(a) that forms the basis for all obviousness rejections set forth in this Office action:

> ***A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.***

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR §1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § *102*(f) or (g) prior art under 35 U.S.C.§ 103(a).

15. Claims 96-116 and newly presented Claims 127-129 are rejected under 35 U.S.C. §103(a) as obvious over Quelle et al. (Blood. 1989. Volume 74, Pgs. 652-657) with evidence provided by Dorland's Illustrated Medical Dictionary (W.B. Saunders Co., Philadelphia, 1988, Page 581)

In response to rejections to claims 96-116 under 35 U.S.C. § 103 (a) cited *supra* in Office Action mailed 30 December 2005, applicants argue that Quelle et al, alone or in combination with any other reference do not teach, "provide any suggestion, motivation or incentive to modify to allow one of skill in the art to arrive at the present invention" and therefore do not

render the instantly claimed invention unpatentable/obvious. Applicants' additional arguments have been detailed and discussed above in item 12.

In view of the discussion presented in item 12 above and side by side comparison of claimed in claims 96-116 and newly presented Claims 127-129 with the teachings from Quelle et al. in the Table presented above, and given the broadest possible interpretation of claims as presented currently, it is clear that Quelle et al. teach a similar product prepared in the same manner and having the same activity (i.e., 200,000 U/mg) as disclosed in the claimed invention. Therefore, the product would intrinsically function in the same, or essentially the same manner as in the claimed invention. Instantly claimed higher purity of said erythropoietin is already taught in Quelle et al. Furthermore, said higher purity is deemed merely a matter of judicious selection and routine optimization of a result effective parameter, which is well within the purview of the skilled artisan. Therefore, the product disclosed in Quelle et al. would intrinsically stimulate erythropoietic activity even with "little *in vivo* activity".

The advantage of further purifying a partially purified protein/hormone for which receptors have been recognized and for which a use is known in the art provide sufficient reason to find the purified protein/hormone to have been obvious to one of ordinary skill in the art at the time of the instantly claimed invention. Some of the advantages of the purification being that the purified protein/hormone:

(i) are more storage-stable;
(ii) generally exhibit an increased specific activity;
(iii) are amenable to amino acid sequencing;
(iv) amino acid sequencing leads to recombinant means of protein/hormone production as is the instant case;
(v) accompanying savings in cost; and
(vi) allow for ready separation of reaction products as compared to separation that must account for impurities.

The above-stated advantages of purification are well known to the artisan of ordinary skill. Such knowledge may provide the suggestion to modify the explicit teachings of the relied upon reference or to combine references. See Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 297 n.24, 227 USPQ 657, 667 n.24 (Fed. Cir. 1985). The position taken is that well known purification techniques would be employed with a reasonable expectation of success in providing a purified product possessing

the claimed properties. Thus, an "obvious to try" standard is not being applied herein. See In re O'Farrell, 853 F.2d 894, 903-904, 7 USPQ2d 1673, 1681 (Fed.Cir. 1988). Additionally, the instantly claimed invention is a product-by-process. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. According to MPEP§2113, "even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior art product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (Citations omitted). In instant invention, the claimed erythropoietin product is clearly documented in the cited prior art.

However, if there is an unexpected result/property or feature of the claimed erythropoietin that has not been made of record and would be obtained by preparing said erythropoietin in the manner that applicants have prepared despite the fact that according to claims as currently presented, the claimed erythropoietin has been prepared in a baculovirus expression system in cultured insect cells, applicants need to make that information of record.

Also note that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art at the time the invention was made. See *In re Keller* 642. F. 2d 413, 208 USPQ 871 (CCPA 1981). Thus, although the Examiner-cited references by themselves may not teach every component in the same order or manner as claimed in the claims under prosecution in the instant application, these references are not relied upon exclusively but in combination. Furthermore, the 35 U.S.C. §103 statute does not require that the prior art identically disclose or describe Applicants' invention but rather that no patent should be obtained if the subject matter as a whole would have been obvious to persons having ordinary skill in this art at the time the invention was made. In this case, given the teachings from Quelle et al. together with those from Dorland's Illustrated Medical Dictionary, the claimed invention would have been obvious to a person of ordinary skill at the time the claimed invention was made.

Applicants' arguments cited *supra* have been fully and carefully considered, but are not persuasive for the reasons of record at Pages 3-6, items 9-10 of the Office Action mailed 30 December 2005 and further for the reasons explained in the preceding paragraph.

In response to applicants' argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, those reasons are cited at Pages 3-6, items 9-10 of the Office Action mailed 30 December 2005 and for additional reasons as discussed *supra*. Furthermore, a rejection under 35 U.S.C. § 103 (a) based upon the combination of references is not deficient solely because the references are combined based upon a reason or technical consideration which is different from that which resulted in the claimed invention (*Ex parte Raychem Corp*, 17 U.S.P.Q. 2d 1417).

In response to applicants' arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

CONCLUSION

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

17. For the aforementioned reasons, no claims are allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached at (571)-272-0925 Monday through Thursday 7:30 A.M. to 6:00 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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April 23, 2007

DAVID M. NAFF
PRIMARY EXAMINER
ART UNIT 1657